

Tourneferon, a New Eudesmanolide from Sagebrush *Artemisia tournefortiana* Rchb.

N. TALZHANOV¹, M. A. RODICHEV¹, V. A. RALDUGIN², YU. V. GATILOV², M. M. SHAKIROV², S. A. IVASENKO¹, K. M. TURDYBEKOV¹ and S. M. ADEKENOV¹

¹Scientific and Industrial Centre “Phytochemistry”,
Ul. Botanicheskaya 12, Karaganda 100009 (Kazakhstan)

E-mail: arglabin@phyto.kz

²Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences,
Pr. Akademika Lavrentyeva 9, Novosibirsk 630090 (Russia)

Abstract

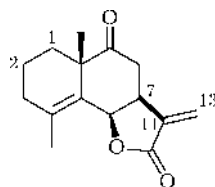
A new sesquiterpene lactone of eudesmane series has been excreted from a tournefortia sagebrush (*Artemisia tournefortiana* Rchb.). The structure of the lactone has been found by the XRD analysis method.

The genus sagebrush (*Artemisia* L.) prevails over all geographical and ecological zones and includes more than 500 species. According to literary data, European, Caucasian, and Central Asian species of sagebrush are most common within the limits of CIS. 82 species from them grow on the territory of Republic Kazakhstan, and they take one of the most outstanding places in formation of the grassy cover [1].

As we continued a systematic research of representatives of the Kazakhstan population of the given genus that is characterized by the presence of sesquiterpene lactones [2, 3], we pioneered in implementation of chemical study of tournefortia sagebrush (*Artemisia tournefortiana* Rchb.).

When studying its overhead part that had been collected in July 2005 in Shet district (Karaganda Region) in its budding phase, a new sesquiterpene lactone that we called “Tourneferon” has been excreted. According to a high-resolution mass spectrum, its gross formula corresponds to C₁₅H₁₈O₃. The IR spectrum of the excreted compound has absorption bands that account for an available butenolide ring, non-conjugated carbonyl group, and double bonds. According to ¹³C NMR spectrum, the molecule of the investigated lactone also includes a tetra-replaced double bond that is non-conjugated with a carbonyl group. To make a reliable

determination of the structure of this lactone, we have conducted its X-ray diffraction analysis and have established that its chemical constitution is given by formula **1** (Fig. 1). It constitutes 9-oxo-6 α (H),7 α (H)-eudesm-4,11(13)-diene-12,6-olide.



Bond lengths in the molecule **1** agree with their statistically average values [4]. The *cis*-jointed lactone cycle is planar, with the standard deviation of atoms from the plane that is 0.036 Å. The conformation of C5–C10 cycle is close to “bath”, deviations of atoms C5 and C8 from the plane of the remaining atoms comprise 0.481(4) and 0.621(5) Å, respectively. The cycle C1–C5, C10 is in a conformation of the deformed “semi-chair”; the respective deviations of atoms C1 and C2 are equal to 0.515(6) and –0.230(6) Å. Among intermolecular contacts, we shall note a slightly reduced [5] contact H...O: (C6) H...O2 2.56 Å. It is interesting to note that the Cambridge base of structural data [6] contains comparatively little data (just 11 of the compounds) about the structure of

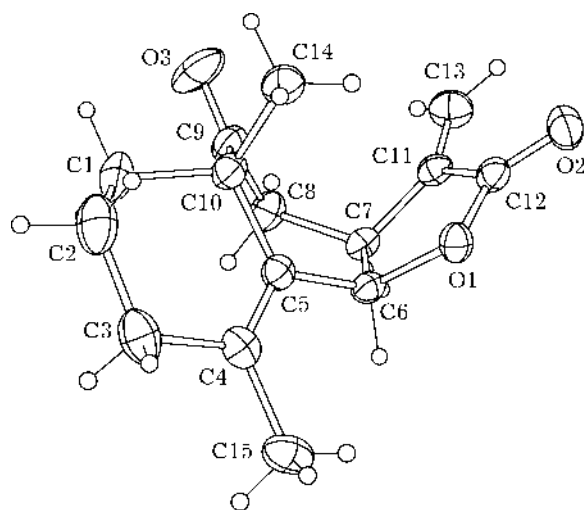


Fig. 1.

6 α (H),7 α (H),10 β (C)-eudesmane-12,6-olides. For the most part they constitute derivatives of santonin [7–10] as well as eudesmane-6,12-olides [11, 12].

We have conducted an interpretation of ^1H and ^{13}C NMR spectra of the lactone **1** (Table 1) with the use of two-dimensional spectra ^1H – ^1H (COSY) and ^{13}C – ^1H (COSY and COLOC).

The melting point was determined with a Boetius device. Optical rotation was measured (at 580 nm) with a Polamat A polarimeter. The IR spectra were recorded with a Avatar 360 FT-IR spectrometer (Thermo Nicolet Corp.,

the USA) in tablets KBr. NMR spectra were recorded with a Bruker DRX-500 spectrometer (the operating frequency was 500.13 and 125.76 MHz for ^1H and ^{13}C , respectively); CDCl_3 was used as a solvent, and TMS, as the internal standard, δ -scale. Column chromatography was conducted on SiO_2 of KSK grade (fractions less than 0.3 mm). Sorbfil plates were applied for thin-layer chromatography, the development by 1 % water solution of KMnO_4 .

Feedstock, namely, the overhead part of *Artemisia tournefortiana* Rchb., was collected in July 2005 in its budding phase in Shetsk district (Karaganda Region, Kazakhstan) and then air-dried.

Excretion of 9-oxo-6 α ,7 α (H)-eudesm-4,11(13)-diene-12,6-olide (1). Raw material, 0.5 kg in mass, was extracted by infusion with 8 L of CDCl_3 at 75 °C. Extraction was repeated four times (4×8 L). The aggregated extracts were filtered off and the solvent was removed in vacuum. The produced solid residue (0.15 kg) was processed three times with EtOH – H_2O (2 : 1) mixture at 70 °C. The deposited ballast matter was separated by decantation; the solution was filtered off. The filtrate was extracted by CHCl_3 (4×0.5 L), chloroformic extractions were aggregated and boiled out to dryness, which resulted in 59 g of a cumulative matter. Using a chromatography of this matter

TABLE 1

Data of ^{13}C and ^1H NMR spectra of the substance **1** (CDCl_3 , δ , ppm, TMS – 0)

<i>i</i>	C_i	H_i	Cross-peaks in two-dimensional spectrum ^{13}C – ^1H COLOC (10 Hz)
1	34.07 t	1.53 m (H-1A); 1.58 m (H-1B)	3H-15; 2H-2
2	17.68 t	1.63 m (H-2A); 1.77 m (H-2B)	2H-3
3	32.24 t	2.13 m (2H)	3H-14
4	139.75 s	–	3H-14
5	128.19 s	–	3H-14; 3H-15; 2H-3
6	75.01 d	5.75 d (4.0)	H-9A; H-13B
7	37.38 d	3.65 m	–
8	40.79 t	2.42 dd (14.0, 3.0); 2.75 dd (14.0, 7.5)	–
9	213.25 s	–	3H-15; H-8A; H-8B; H-7
10	47.09 s	–	3H-15; H-6
11	137.89 s	–	H-8A
12	169.41 s	–	H-6; H-13B
13	123.92 t	5.56 (A) d (2.5); 6.35 (B) d (2.5)	–
14	24.50 q	1.86 (3H, s, Me-4)	–
15	17.68 q	1.17 (3H, s, Me-10)	–

on SiO₂ (the eluent—petroleum ether, a mixture of petroleum ether with ethyl acetate with a gradient increase of the latter from 0 to 20 %), 2 g (0.4 %) of lactone **1** have been extracted in the form of colourless crystals with the m. p. of 170–172 °C, $[\alpha]_D^{20} +29.4^\circ$ (with 0.68 CHCl₃).

The mass spectrum (EA, 70 eV), m/z (I_{rel} , %): 246 (M^+ , 97), 131 (50), 203 (100), 159 (19), 157 (42), 137 (22), 131 (45), 109 (27), 105 (23), 105 (23), 93 (23). The high-resolution mass spectrum, it has been observed (m/z): 246.12831. It has been calculated for C₁₅H₁₈O₃: 246.12559.

IR spectrum (KBr, ν , cm⁻¹): 1740 (C=O of γ -lactone); 1716 (C=O), 1658, 1656 1319, 1278, 1264, 1214, 1145, 953, 863, 818, 677.

X-ray diffraction study has been conducted with Bruker P4 diffractometer (MoK α radiation, a graphite monochromator, $\theta/2\theta$ scanning) at ambient temperature. Corrections for absorption were introduced by an empirical method. The structure was deciphered by a direct method with the SHELXS-97 code and adjusted by a least square method in anisotropic-isotropic approximation with the SHELXS-97 code. Positions of hydrogen atoms were set geometrically and adjusted under an “equestrian” model. Crystallographic data: rhombic syngony, space group $P2_12_12_1$, $a = 6.3648(6)$, $b = 9.2590(8)$, $c = 21.795(2)$ Å, $V = 1284.4(2)$ Å³, C₁₅H₁₈O₃, $Z = 4$, $d_{calc} = 1.274$ g/cm³, $\mu = 0.88$ cm⁻¹, transmission $T_{min}/T_{max} = 0.913/0.979$, a scanning region $2\theta < 52^\circ$, a sample size of $0.17 \times 0.2 \times 0.9$ mm. Adjustment parameters: $wR_2 = 0.1198$, $S = 1.024$ (throughout all 1435 reflections), $R_1 = 0.0410$ ($1192 I \geq 2\sigma(I)$), 163

adjusted parameters. In view of the absence of heavy atom from the molecule under investigation, it was impossible to establish its absolute configuration. The formula **1** specifies a relative configuration of all dissymmetric centres, although it appears that it corresponds also to the absolute configuration in view of $\alpha(H)$ configuration at C7. The results have been deposited at Cambridge Crystallographic Centre (the deposition number CCDC 645287) and they are available free at the address: <http://www.ccdc.cam.ac.uk/cgi-bin/catreq.cgi>

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